REMARKS

Claims 15, 16, 18-23, and 25-28 presently appear in this case. No claims have been allowed. The Official Action of May 8, 2009, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention is directed to a method for selecting a subject having an autoimmune disease that would be suitable for anti-inflammatory treatment by means of an A3 adenosine receptor (A3AR) agonist. From among those subjects in an inflammatory state as a result of the autoimmune disease, those that are candidates for such treatment will have a level of expression of A3AR in a sample of their white blood cells that is above a predefined threshold, i.e., that is above the level of A3AR expression in WBCs of a healthy subject. Those subjects with autoimmune disease that have such an elevated expression level of A3AR are then determined as being suitable to receive such anti-inflammatory therapeutic treatment. Thus, the method of the present invention is not directed to a method of treatment but only to a method of selection. The present invention is also directed to a method for determining the probability that a selected subject in an inflammatory state that is a result of an autoimmune disease will respond to A3AR agonist anti-inflammatory therapeutic treatment. In this method, the level

of expression of A3AR in a sample of white blood cells of the subject is determined and then, if the level of A3AR expression is above a predefined threshold that is above the level of A3AR expression in WBCs of a healthy subject, a determination is made that there is a greater probability that the subject will respond to the anti-inflammatory treatment.

The examiner has made a new restriction requirement between Group III, which includes claims 15-20, and Group IV, which includes claims 22-28. The examiner states that these inventions are directed to two separate and distinct processes as the invention of Group III is directed to a method for selecting a subject in an inflammatory state, which subject is suitable for anti-inflammatory therapeutic treatment by means of an A3 adenosine receptor agonist, whereas the invention of Group IV is directed to a method for determining the probability that a selected subject in an inflammatory state will respond to an anti-inflammatory therapeutic treatment by means of a A3 adenosine receptor agonist. The examiner states that the special technical feature (i.e., A3 adenosine receptor and its agonist) is known in the prior art and that no special technical feature unites the multiple inventions as currently presented. The examiner states that since applicant has received an action on the merits for the claims of originally presented Group III, newly added claims 22-28 have

been withdrawn from consideration as being drawn to a non-elected invention. This new restriction requirement is respectfully traversed.

The examiner is incorrect in stating the special technical feature of the present invention is A3 adenosine receptor and its agonist. That clearly is not the case, as A3 adenosine receptors and their agonists are admittedly well known and applicant is not claiming them, *per se*. The special technical feature of the present invention is the step of relating the level of expression of A3AR in a sample of white blood cells of a subject with the probability that the subject is suitable for anti-inflammatory therapeutic treatment by means of a A3AR agonist. This is common to both sets of claims. In claim 15, a subject is selected as being suitable for anti-inflammatory therapeutic treatment by means of A3AR agonist, while in claim 22, a determination is made that there is a greater probability that that subject will respond to anti-inflammatory therapeutic treatment if the level of expression of A3AR in a sample of WBCs of the subject is greater than that of a healthy subject. Essentially, the same thing is being stated in two different ways. Additionally, the examiner cannot establish that there is a different field of search and that there would be a burden in searching both sets of claims.

The examiner's recollection is drawn to the fact that, in the interview among examiners Singh and Marx and the undersigned attorney conducted on January 16, 2009, the undersigned suggested the possibility of claiming the invention in the way that is now set forth in claim 22, as supported on page 11 of the specification. At the interview, the examiners were receptive to this suggestion and the examiners actually suggested submitting both sets of claims so that the examiners could decide which they considered to be preferable. That is why the previous amendment included two complete sets of claims, 15-21 and 22-28, drawn to the two types of claims discussed at the interview.

While it is apparent that both sets of claims overcome the previous 35 USC §112 rejections, applicant would prefer that both sets of claims remain in the case since they are both claiming the same invention, though viewed from a slightly different perspective, and both include the same special technical feature as discussed above.

Furthermore, there would be no additional burden to search both sets of claims as the field of search would be identical. Certainly, any reference that would be applicable to claim 22 would have been turned up in the course of the examiner's search of claim 15. Accordingly, for all of these reasons, reconsideration and withdrawal of this restriction

requirement and consideration and allowance of all of the claims now present in the case are respectfully urged.

Claims 15-21 have been rejected under 35 USC §103(a) as being unpatentable over Gessi taken with Rhodes and in view of Montesinos and Fishman. The examiner states that Gessi discloses a method for selecting a subject having colorectal cancer, which the examiner notes is associated with inflammation, by determining the level of expression of A3AR in a sample of white blood cells of the subject. The examiner acknowledges that Gessi does not disclose the step of selecting the subject as being suitable to receive anti-inflammatory therapeutic treatment by means of A3AR agonists if the level is above a predefined threshold, nor does Gessi talk about selecting subjects having an inflammatory state that is a result of an autoimmune disease, such as rheumatory arthritis. The examiner states that Fishman discloses the pharmacology and therapeutic applications of A3AR agonists such as IB-MECA for the treatment of inflammation and Montesinos disclose the role of A3AR receptors, the activation of which is required for the inhibition of inflammation in inflammatory diseases such as rheumatory arthritis. The examiner concludes that it would be obvious to modify the method of Gessi such that the subject is selected as being suitable to receive the anti-inflammatory treatment by means

of an A3AR agonist, if the level is above a predetermined threshold and where in the inflammatory state as the result of an autoimmune disease such rheumatory arthritis. The examiner states that those of ordinary skill would have been motivated to do such modification in the method of Gessi, because the disclosures of Fishman and Montesinos implicate A3AR receptor activation and its role in anti-inflammatory treatment in patients with inflammation, such as RA, using IB-MECA with a reasonable expectation of success. Thus, the examiner concludes that such an artisan would have fully contemplated the implications and teachings from the cited prior art that provide the nexus between the overexpression of A3AR receptor and peripheral white blood cells as taught by Gessi and inflammatory state of a subject that is suitable to receive the anti-inflammatory treatment. This rejection is respectfully traversed.

The present claims have now been amended to be specifically directed to selecting subjects suitable for treatment of an autoimmune inflammatory disease. Thus, the subject matter of previously appearing claims 17 and 24 have now been inserted in the claims from which they depended.

Gessi is limited to the description of the higher density of A3AR in colon carcinomas as compared to normal mucosa originating from the same individual or from healthy

subjects and concludes that this overexpression of the A3AR at the protein level can be used as a diagnostic marker or therapeutic target for colon cancer. However, the present claims have now been limited to selection of subjects suitable for treatment of an autoimmune inflammatory disease. Autoimmune inflammatory diseases cannot be considered the same as colon carcinoma and the behavior of the A3AR in an the white blood cells of a patiet with an autoimmune inflammatory disease cannot be deduced from its behavior in cancer, as the latter does not involve an autoimmune response.

While Fishman and Montesinos relate to the use of an A3AR agonist in the treatment of autoimmune diseases, there is no suggestion therein that the level of A3AR expression in white blood cells of autoimmune patients may be used as a diagnostic for the presence of autoimmune disease, as Gessi does with respect to colon carcinoma. Certainly, there is no suggestion that patients already in an inflammatory state can be selected as being suitable to receive anti-inflammatory treatment using an A3AR agonist when the level of expression of A3AR in the WBCs of the subject is above a predefined threshold that is above the level of A3AR expression in WBCs of healthy subjects. This is nowhere taught or suggested by any combination of the references of record.

The most recent Supreme Court pronouncement on obviousness is *KSR International v. Teleflex Inc.*, 550 U.S. 398, 127 S.Ct. 1727, 82 USPQ2d 1385 (2007). Note where the Court, 127 S.Ct. at 1741, cited with approval the following statement from *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006):

> Rejections on obviousness grounds cannot be sustained by mere conclusary statements; instead, there must be some articulated reasoning with rational underpinning to support the legal conclusion of obviousness.

Note also where the Court stated at 1742:

> A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning.

Simply said, the examiner has not submitted the articulated reasoning with rational underpinning that is necessary to support the legal conclusion of obviousness required by *KSR*.

Accordingly, the method of selecting an autoimmune disease patient that is most suitable for treatment with an A3AR agonist is nowhere taught or suggested by any of the references of record, either alone or in combination. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of

record and fully comply with 35 USC §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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